Fakultät für Medizin

Dokumenttyp: journal article

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Titel des Beitrags:
Primary glioblastoma cultures: can profiling of stem cell markers predict radiotherapy sensitivity?

Abstract:
Human glioblastomas may be hierarchically organized. Within this hierarchy, glioblastoma-initiating cells have been proposed to be more resistant to radiochemotherapy and responsible for recurrence. Here, established stem cell markers and stem cell attributed characteristics such as self-renewal capacity and tumorigenicity have been profiled in primary glioblastoma cultures to predict radiosensitivity. Furthermore, the sensitivity to radiotherapy of different subpopulations within a single primary glioblastoma culture was analyzed by a flow cytometric approach using Nestin, SRY (sex-determining region Y)-box 2 (SOX2) and glial fibrillary acidic protein. The protein expression of Nestin and SOX2 as well as the mRNA levels of Musashi1, L1 cell adhesion molecule, CD133, Nestin, and pleiomorphic adenoma gene-like 2 inversely correlated with radioresistance in regard to the clonogenic potential. Only CD44 protein expression was correlated positively with radioresistance. In terms of proliferation, Nestin protein expression and Musashi1, pleiomorphic adenoma gene-like 2, and CD133 mRNA levels are inversely correlated with radioresistance. Higher
expression of stem cell markers does not correlate with resistance to radiochemotherapy in the cancer genome atlas glioblastoma collective. SOX2 expressing subpopulations exist within single primary glioblastoma cultures. These subpopulations predominantly form the proliferative pool of the primary cultures and are sensitive to irradiation. Thus, profiling of established stem cell markers revealed a surprising result. Except CD44, the tested stem cell markers showed an inverse correlation between expression and radioresistance. Markers used to define glioma-initiating cells (GIC) are generally not defining a more resistant, but rather a more sensitive group of glioma cells. An exemption is CD44 expression. Also proliferation of the GIC culture itself was not systematically associated with radiosensitivity or - resistance, but a SOX-2 positive, proliferative subgroup within a GIC culture is showing the highest radiosensitivity.